AMENDMENTS

Amendments to the Specification:

At page 14, lines 13 through 20, please replace with the following paragraph:

FIG. 4. Tactics for competitive RT-PCR™ with COP primers. The portion of the HSP27 cDNA sequence (SEQ ID NO:4) indicated with the heavy underline below can be amplified by the standard primers COP 32 (SEQ ID NO:3) and COP 46 (SEQ ID NO:5). Primer CRT004, containing the COP 32 sequence, a 5 bp insert (identified by the box), and the next 8 bp from HSP27 ("clamp" sequence, identified by overline) were synthesized. When CRT004 (SEQ ID NO:6) and COP 46 were used in a PCR™ reaction containing the HSP27 template, an amplimer identified as CRT32/46 (SEQ ID NO:7) was produced. As CRT32/46 contains all of the HSP27 sequences plus the 5 bp insert it can be used as a competitive template.

At page 15, lines 14 through 21, please replace with the following paragraph:

FIG. 8. Partial sequence of MLN 62 mRNA. Primers for COP are highlighted, and the poly(A) addition signal sequence is underlined. The A-end primer sequence (CATGCCTT), starting at position 1760, contains the CATG that is closest to the 3′ end of the mRNA. The highlighted B-end primer sequence (TGAGATC), starting at position 1880, contains the first GATC following the A-end primer. Note that the actual B-end primer contains the reverse complement of the highlighted sequence (GATCTCA) (SEQ ID NO:8). This decreases the number of positions queried at the B-end by one, thus reducing the number of experiments by a factor of four.

At page 32, lines 5 through page 36, please replace Table 1 with the following Table 1:

TABLE 1: RESTRICTION ENZYMES

Enzyme Name	Recognition Sequence	SEQ ID NO:
AatII	GACGTC	
Acc65 I	GGTACC	

Acc I	GTMKAC	
Aci I	CCGC	
Acl I	AACGTT	
Afe I	AGCGCT	
Afl II	CTTAAG	
Afl III	ACRYGT	
Age I	ACCGGT	
Ahd I	GACNNNNNGTC	9
Alu I	AGCT	
Alw I	GGATC	
AlwN I	CAGNNNCTG	
Apa I	GGGCCC	
ApaL I	GTGCAC	
Apo I	RAATTY	
Asc I	GGCGCGCC	
Ase I	ATTAAT	
Ava I	CYCGRG	
Ava II	GGWCC	
Avr II	CCTAGG	
Bae I	NACNNNNGTAPyCN	10
BamH I	GGATCC	
Ban I	GGYRCC	
Ban II	GRGCYC	
Bbs I	GAAGAC	
Bbv I	GCAGC	
BbvC I	CCTCAGC	
Bcg I	CGANNNNNNTGC	11
BciV I	GTATCC	
Bcl I	TGATCA	
Bfa I	CTAG	
Bgl I	GCCNNNNNGGC	12
Bgl II	AGATCT	
Blp I	GCTNAGC	
Bmr I	ACTGGG	
Bpm I	CTGGAG	
BsaA I	YACGTR	
BsaB I	GATNNNNATC	13
BsaH I	GRCGYC	
Bsa I	GGTCTC	
BsaJ I	CCNNGG	
BsaW I	WCCGGW	
BseR I	GAGGAG	
Bsg I	GTGCAG	
BsiE I	CGRYCG	
BsiHKA I	GWGCWC	
BsiW I	CGTACG	

Bsl I	CCNNNNNNNGG	14
BsmA I	GTCTC	
BsmB I	CGTCTC	
BsmF I	GGGAC	
Bsm I	GAATGC	
BsoB I	CYCGRG	
Bsp1286 I	GDGCHC	
BspD I	ATCGAT	
BspE I	TCCGGA	
BspH I	TCATGA	
BspM I	ACCTGC	
BsrB I	CCGCTC	
BsrD I	GCAATG	
BsrF I	RCCGGY	
BsrG I	TGTACA	
Bsr I	ACTGG	
BssH II	GCGCGC	
BssK I	CCNGG	
Bst4C I	ACNGT	
BssS I	CACGAG	
BstAP I	GCANNNNNTGC	15
BstB I	TTCGAA	
BstE II	GGTNACC	
BstF5 I	GGATGNN	
BstN I	CCWGG	
BstU I	CGCG	
BstX I	CCANNNNNNTGG	16
BstY I	RGATCY	
BstZ17 I	GTATAC	
Bsu36 I	CCTNAGG	
Btg I	CCPuPyGG	
Btr I	CACGTG	
Cac8 I	GCNNGC	
Cla I	ATCGAT	
Dde I	CTNAG	
Dpn I	GATC	
Dpn II	GATC	
Dra I	TTTAAA	
Dra III	CACNNNGTG	
Drd I	GACNNNNNNGTC	17
Eae I	YGGCCR	
Eag I	CGGCCG	
Ear I	CTCTTC	
Eci I	GGCGGA	
EcoN I	CCTNNNNNAGG	18
EcoO109 I	RGGNCCY	

EcoR I	GAATTC	
EcoR V	GATATC	
Fau I	CCCGCNNNN	
Fnu4H I	GCNGC	
Fok I	GGATG	
Fse I	GGCCGGCC	
Fsp I	TGCGCA	
Hae II	RGCGCY	
Hae III	GGCC	
Hga I	GACGC	
Hha I	GCGC	
Hinc II	GTYRAC	
Hind III	AAGCTT	
Hinf I	GANTC	
HinP1 I	GCGC	
Hpa I	GTTAAC	
Hpa II	CCGG	
Hph I	GGTGA	
Kas I	GGCGCC	
Kpn I	GGTACC	
Mbo I	GATC	
Mbo II	GAAGA	
Mfe I	CAATTG	
Mlu I	ACGCGT	
Mly I	GAGTCNNNNN	19
Mnl I	CCTC	
Msc I	TGGCCA	
Mse I	TTAA	
Msl I	CAYNNNNRTG	20
MspA1 I	CMGCKG	
Msp I	CCGG	
Mwo I	GCNNNNNNGC	21
Nae I	GCCGGC	
Nar I	GGCGCC	
Nci I	CCSGG	
Nco I	CCATGG	
Nde I	CATATG	
NgoMI V	GCCGGC	
Nhe I	GCTAGC	
Nla III	CATG	
Nla IV	GGNNCC	
Not I	GCGGCCGC	
Nru I	TCGCGA	
Nsi I	ATGCAT	
Nsp I	RCATGY	
Pac I	TTAATTAA	

PaeR7 I	CTCGAG	
Pci I	ACATGT	
PflF I	GACNNNGTC	
PflM I	CCANNNNNTGG	22
PleI	GAGTC	
Pme I	GTTTAAAC	
Pml I	CACGTG	
PpuM I	RGGWCCY	
PshA I	GACNNNNGTC	23
Psi I	TTATAA	
PspG I	CCWGG	
PspOM I	GGGCCC	
Pst I	CTGCAG	
Pvu I	CGATCG	
Pvu II	CAGCTG	
Rsa I	GTAC	
Rsr II	CGGWCCG	
Sac I	GAGCTC	
Sac II	CCGCGG	
Sal I	GTCGAC	
Sap I	GCTCTTC	
Sau3A I	GATC	
Sau96 I	GGNCC	
Sbf I	CCTGCAGG	
Sca I	AGTACT	
ScrF I	CCNGG	
SexA I	ACCWGGT	
SfaN I	GCATC	
Sfc I	CTRYAG	
Sfi I	GGCCNNNNNGGCC	24
Sfo I	GGCGCC	
SgrA I	CRCCGGYG	
Sma I	CCCGGG	
Sml I	CTYRAG	
SnaB I	TACGTA	
Spe I	ACTAGT	
Sph I	GCATGC	
Ssp I	AATATT	
Stu I	AGGCCT	
Sty I	CCWWGG	
Swa I	ATTTAAAT	
Taq I	TCGA	
Tfi I	GAWTC	
Tli I	CTCGAG	
Tse I	GCWGC	
Tsp45 I	GTSAC	

Tsp509 I	AATT	
TspR I	CAGTG	
Tth111 I	GACNNNGTC	
Xba I	TCTAGA	
Xcm I	CCANNNNNNNNNTGG	25
Xho I	CTCGAG	
Xma I	CCCGGG	
Xmn I	GAANNNNTTC	26

At page 53, lines 5 through 20, please replace with the following paragraph:

2. Specificity Of COP

As an example of the specificity of the method, reactions were performed with primers predicted to produce a 291 bp amplimer from the murine *Brca1* gene. As template for these reactions, mRNA was prepared from cultures of mouse keratinocytes. Epidermal keratinocyte cultures were derived from newborn mice and maintained as described, Pierce *et al.,* 1998a. Total RNA was prepared by extraction into a chaotropic salt solution and organic solvent extraction using either a QIAGEN (Valencia, CA). mRNA was prepared using a QIAGEN kit, and double-stranded cDNA was synthesized using a GIBCO/BRL kit but substituting biotinylated $p(dT)_{18}$ as the primer for first strand synthesis. Double stranded linkers with overhangs complementary to the ends created by restriction with Nla III (A-linker) and Dpn II (B-linker) were prepared separately by mixing equal amounts of the following oligonucleotides, warming to 90°C for 2 min and slowly cooling to room temperature: A-linker - 5′-CGTCTAGACAGC (SEQ ID NO:27) (previously phosphorylated with T4 polynucleotide kinase) and 5′- GCTGTCTAGACGCATG (SEQ ID NO:28); B-linker - 5′ - CGGTGATGCATC (SEQ ID NO:29) and 5′ -GATCGATGCATCACCG (SEQ ID NO:30) (previously phosphorylated with T4 polynucleotide kinase).

At page 54, lines 3 through 11, please replace with the following paragraph:

To test the selectivity of the method, two pairs of primers that differed by a single nucleotide from the *Brca1* primers were also chosen that were expected to produce amplimers of 117 and 197 bp from the genes for annexin III and an anonymous cDNA (clone 2C11B), respectively. Two sets of primers for COP PCR™ reactions were synthesized, corresponding to

the A- and B- linkers above, but containing 3 or 4 nucleotide specificity regions at the 3' end. The sequences of these primer sets were:

A-end (256 primers)-5'-GCTGTCTAGACGCATGNNNN (SEQ ID NO:31);
B-end (64 primers)-5'-CGGTGATGCATCGATCNNN (SEQ ID NO:32).

At page 69, lines 1 through 18, please replace with the following paragraph:

was adsorbed to magnetic beads coated with streptavidin (Dynal, Lake Success, NY) and non-biotinylated fragments were washed from the beads. cDNA fragments still bound to the beads were ligated to the B-linker; then digested with Nla III; and fragments released from the beads by this treatment were selected and ligated to the A-linker. Double stranded linkers with overhangs complementary to the ends created by restriction with Nla III (A-linker) and Dpn II (B-linker) were prepared separately by mixing equal amounts of the following oligonucleotides: warming to 90°C for 2 min and slowly cooling to room temperature: A-linker - 5'-CGTCTAGACAGC (SEQ ID NO:27) (previously phosphorylated with T4 polynucleotide kinase) and 5'-GCTGTCTAGACGCATG (SEQ ID NO:28); B-linker - 5' - CGGTGATGCATC (SEQ ID NO:29) and 5' - GATCGATGCATCACCG (SEQ ID NO:30) (previously phosphorylated with T4 polynucleotide kinase). Linkers (217 ng) were added to restricted cDNA fragments (initially 1.5 μg), warmed to 50°C for 2 min, cooled to room temperature for 15 min, then cooled on ice. Ligation was accomplished by adding 10 U T4 DNA ligase (GIBCO/BRL) and incubating in a final volume of 50 μL for 2h at 16°C. These fragments of cDNA, containing the gene-specific targets ligated to the B and A linkers, are referred to as B/A genetags. A second preparation, A/B genetags, is obtained when Nla III restriction and A-linker ligation preceded the Dpn II restriction and B-linker ligation. Also refer to FIG. 1.

Please delete the current Sequence Listing and insert therefor the Substitute Sequence Listing numbered pages 1 to 11 as submitted electronically herewith as text.